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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,530	04/07/2004	Dennis Benjamin	PPI-144	8326

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EXAMINER	
PERREIRA, MELISSA JEAN	

ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/820,530	BENJAMIN ET AL.	
	Examiner	Art Unit	
	Melissa Perreira	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-18 and 26 are pending in the application. Claims 19-25 were cancelled in the amendment filed 4/13/07. Any objections and/or rejections from previous office actions that have not been reiterated in this office action are obviated.

Response to Arguments

1. Applicant's arguments filed 4/13/07 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-3,9 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention as stated in the office action mailed 10/13/06. It is unclear as to which test compound or biological target to use for the method of measuring the ability of a test compound to inactivate a biological target in the instant claims 1-3,9 and 10. The administration of different compound will vary with regards to dose or the biological target of interest. The recitation of a "test compound which is an inhibitor of a biological target" does not impart any physical or structural characteristics necessary for the test compounds of the instant claims.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-18 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear as to what parts of a biological sample constitutes "fractions thereof" or "portions thereof". It is confusing as to the amount of biological material required of each fraction/portion. Also, the necessary structural/physical characteristics of the fraction or portions of the biological sample, such as a whole cell or individual cell components to carry out the invention of the instant claims are not provided.

6. Claims 3 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear as to what constitutes a "saturating amount" as there are multiple levels/definitions of saturation, such as saturated to the point in which a solution can dissolve no more of a substance, supersaturation where the concentration of a substance in a solution is higher than the saturation point and in biochemistry saturation refers to the fraction of total protein binding sites that are occupied at a given time. The specification does not provide any guidance as to the definition of saturating amount.

7. Claims 3 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear as to how much constitutes "substantially all of the free biological target reacts". The specification does not provide any guidance as to determine how much is a substantial amount.

8. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 26 recites the broad recitation test compound which is an inhibitor of MetAP-2, and the claim also recites the MetAP-2 inhibitor is of the structure provided which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Turk et al. (*Chem. Biol.* **1999**, *6*, 823-833) in view of Soker et al. (US 2005/0112063A1).

11. Turk et al. (*Chem. Biol.* **1999**, *6*, 823-833) discloses the treatment of bovine aortic endothelial cells with fumagillin analog, TNP-470 that are then lysed for determination of unbound MetAP2. These lysates were treated with biotin-fumagillin, labeling MetAP2 protein that remained unbound following TNP-470 treatment. Bound biotin was detected by probing the membrane with streptravidin-horseradish peroxidase, and the signal was competed by cell treatment with increasing concentrations of TNP-470 (p824, results). The inhibition of MetAP2 was examined in several human cell lines, such as HeLa, Jurkat T lymphocytes and HT1081C (p825, paragraph 1). Turk et al. (*Chem. Biol.* **1999**, *6*, 823-833) does not teach of the administration of the fumagillin analog to a subject or removing biological samples from the subject.

12. Soker et al. (US 2005/0112063A1) discloses the method of measuring the ability of a test compound to inhibit a biological target via the administration of an antiangiogenic compound, such as a polymer conjugated TNP-470 to a subject in vitro or in vivo and assessing the bioeffectiveness of the compound (p2, [0014] and [0020];

p10, [0109]). The method of measuring the ability of the polymer conjugated TNP-470 to inhibit the formation of blood vessels is by measuring the level of protein in a biological sample, such as the bodily fluid blood (p2, [0020]). The measurement of the sample after administration of the polymer conjugated TNP-470 is compared to a control sample taken prior to administration of the polymer conjugated TNP-470 (p2, [0020]). Also the effects of the polymer conjugated TNP-470 can be examined for the inhibition of liver regeneration compared to a control via hepatectomy (p3, [0029]; p9, [0100]; p10, [0106]).

13. At the time of the invention it would have been obvious to one ordinarily skilled in the art to use the method of measuring the inhibition of MetAP2, such as disclosed by Turk et al. by administering the fumagillin analog to a subject (in vivo) then collecting the blood and/or liver tissue samples and examining the samples for inhibition (Soker et al.). The use of the polymer conjugated TNP-470 is advantageous as the TNP-470 is not water-soluble but becomes water-soluble following conjugation with the polymer (Soker et al., p10, [0103]).

14. Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffiths et al. (*Proc. Natl. Acad. Sci.* **1998**, *95*, 15183-15188) in view of Soker et al. (US 2005/0112063A1).

15. Griffiths et al. (*Proc. Natl. Acad. Sci.* **1998**, *95*, 15183-15188) discloses the incubation of recombinant human MetAP2 with ovalicin followed by incubation with fluorescein-fumagillin analog. The samples were dialyzed, alkylated, digested and

subjected to HPLC separation. The absorbance of each eluate was monitored and the fractions corresponding to peaks for the binding of the fluorescein-fumagillin analog to the MetAP2 were collected (p15184, identification of the covalently modified MetAP2 residue by using fluorescein-fumagillin). It is disclosed that fumagillin and ovalicin covalently bind and inhibit MetPA2 (abstract). Griffiths et al. (*Proc. Natl. Acad. Sci.* **1998**, *95*, 15183-15188) does not disclose the administration of ovalicin, a fumagillin analog to a subject or removal of a biological sample from a subject.

16. Soker et al. (US 2005/0112063A1) discloses the method of measuring the ability of a test compound to inhibit a biological target via the administration of an antiangiogenic compound, such as a polymer conjugated TNP-470 to a subject in vitro or in vivo and assessing the bioeffectiveness of the compound as well as that stated above.

17. At the time of the invention it would have been obvious to one ordinarily skilled in the art to utilize the method to identify the binding/inhibition of MetAP2 to/by a quantifiable irreversible inhibitor, such as fluorescein-fumagillin, Griffiths et al. by administering the fumagillin analog to a subject (in vivo) then collecting the blood and/or liver tissue samples and examining the samples for inhibition (Soker et al.). The use of the polymer conjugated TNP-470 is advantageous as the TNP-470 is not water-soluble but becomes water-soluble following conjugation with the polymer (Soker et al., p10, [0103]).

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa Perreira whose telephone number is 571-272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MP
May 10, 2007

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER